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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,069	10/04/2004	Mark T. Bilodeau	21074YP	5612

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EXAMINER	
TUCKER, ZACHARY C	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 11/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/510,069	BILODEAU ET AL.	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,24 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20Dec04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first and second paragraphs of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
>
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-17, 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Treating "cancer," generally, as is recited in claims 15-17, 24 and 25, and, according to the instant specification, is embraced by the language of claims 12-14, is not enabled solely on the reliance of assay testing for inhibition of the activity of one or more isoforms of Akt. While Akt may be implicated in the development of certain cancers as discussed in the Nakatani et al and Bellacosa et al references, cited in applicants' Information Disclosure Statement filed 20 December 2004, there was no basis in the prior art at the time of applicants' effective filing that any Akt inhibitor much less Akt inhibitors as a class were known to treat any and all cancers. It is noted that claim 24 specifies the prevention of cancer, generally, as well as the treatment of cancer.

The following review:

> Hanada et al, "Structure regulation and function of PKB/AKT - a major therapeutic target" Biochimica et Biophysica Acta vol. 1697, pages 3-16 (2004).

Which was actually published more recently than the Nakatani et al and Bellacosa et al references, evidences that research in the therapeutic or clinical use of Akt inhibitors is in the preliminary stages (see "Conclusions," page 12-13).

The criteria for determination of whether or nor a claimed invention is enabled as set out in *In re Wands*, 858 F.2d 731,737 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), includes factors such as:

1. Level of unpredictability in the art – The invention is pharmaceutical in nature, involving inhibition of one or more kinases of which many types currently exist with differing biological functions as discussed in the above-referenced Nakatani et al and Bellasco et al references. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be unpredictable. See *In re Fisher* 166 USPQ 18.

2. Direction or guidance – The amount of guidance presented in the specification as to which compounds are sufficiently active to be useful in the claimed methods is nonexistent.

3. Working examples – The test data presented is for an assay testing which is not art-recognized as being reasonably predictive of *in vivo* efficacy. Thus, in the absence of animal studies and in the absence of any practical correlation between studies conducted in vitro and the expansive scope of the diseases to be treated, there is no sufficient evidence to support the claimed methods of treating and preventing cancer.

4. Level of skill in the art – The area directed to Akt inhibition is experimental, with no indication of any drugs having Akt-inhibiting activity actually known to treat one or more cancers. Therefore the level of skill is low. If applicants disagree, they

are invited to provide evidence to contrary, showing that at the time of applicants' filing date one more cancers would be reasonably treatable in man, the intended subject of the method according to instant claims 12-17, 24 and 25

Where the assertion of utility is unusual, difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are viewed as being reasonably predictive of *in vivo* efficacy by those of ordinary skill in the art. See, for example, *In re Ruskin* 148 USPQ 221; *Ex parte Jovanovics* 211 USPQ 907 (MPEP 2164.05(a)).

Claims 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The method according to claims 12-14, in addition to lacking enablement as outlined *supra*, is indefinite in scope because exactly for what the therapeutically effective amount of the compound of claim 1, claim 6 or claim 8 is effective for is not ascertainable from reading said claims in light of the specification.

Although applicants' specification describes treatment of cancer as being the primary therapeutic utility, the full scope of *all* therapies contemplated by the language of claims 12-14 is undefined.

The most specific statement relating to what types of conditions or diseases *in addition to* cancer are treated by a method of "inhibiting one or more isoforms of Akt in a mammal" which appears at page 2 in the specification is:

> These observations demonstrate that the PI3K/Akt pathway plays important roles for regulating cell survival or apoptosis in tumorigenesis.

Clearly, there is no specific group of diseases or medical conditions for which inhibition of one or more isoforms of Akt is therapeutically effective, according to applicants' specification.

Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-18, 24 and 25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-41 of copending Application No. 10/510,068. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of the copending application are drawn to methods for treating cancer, the preferred embodiments of which include the administration of a compound according to the present invention. No molecular structure diagram is included in the claims of the copending application, however, if one of ordinary skill were to consult the specification in order to ascertain what chemical compounds are

contemplated by the limitation "a selective inhibitor of the activity of one or more isoforms of Akt," which is recited in all claims of the copending application, he would at once envision a compound as is set forth in the claims of the instant application. Specifically, at pages 41-46 of the specification of the copending application, Akt inhibitors of the formula VII are described, which formula VII correlates exactly with "Formula A" as set forth in instant claim 1, from which all of the other instant claims (save claim 6) depend. Lines 17 and 18, page 76 of the copending application describe one of the preferred species of the Akt inhibitors employed in the methods according to the copending application, and that specie is the same compound as the second named compound in instant claim 6. Hence, if the claims of the copending application were prior art, all of the instant claims would be anticipated by those claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

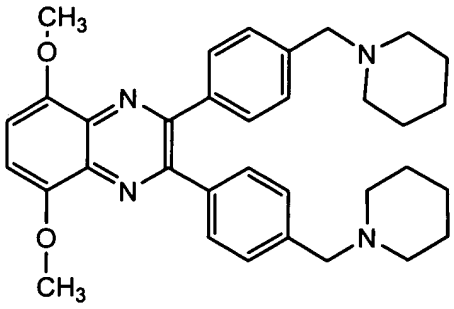
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 9 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by either Indian Journal of Chemistry, vol. 30B, pages 777-783 (1991) or IN 166761, both Venugapalan et al.

Both the Indian patent and the journal article (cited by applicants in the Information Disclosure Statement filed 20 December 2004) disclose as an ameobicide the compound

2,3-*bis*-(4-piperidinomethylphenyl)-5,8-dimethoxyquinoxaline, which has the structure shown here:



The Indian Journal of Chemistry article reports the synthesis of this compound in the experiment bridging columns 1 and 2 of page 781, while the Indian patent discloses the compound for example at page 2, third line up from the bottom of the page, and at pages 16-17, in the figures – the reference compound is "Formula I, figure 5."

The compound which is represented by the above-diagrammed structure anticipates instant claim 1 wherein u, v, w and x are all CH; both y and z are N; "Q" is aryl (phenyl); p=1 and R^2 is alternative "1)," where a=0, b=0, and (C_1-C_{10})alkyl is C_1 alkyl (methyl), substituted with one R^z, where R^z is alternative "12)," where r=0, s=0 and (C_0-C_6)alkylene is C_0 alkylene and "heterocyclyl" is piperidin-1-yl; n=2 and R^1 is alternative "1)," where a=0, b=1, and (C_1-C_{10})alkyl is C_1 alkyl (methyl) – forming two methoxy groups.

Venugapalan et al, the journal article, discloses a pharmaceutical composition according to instant claim 9 and a method according to instant claim 12. On page 780, animal studies with the compounds reported in that reference are disclosed. It is by virtue of compound number 15 having been employed in one of the animal experiments that a pharmaceutical composition was necessarily disclosed and a method of inhibiting at least

one isoform of Akt, by administering a therapeutically effective amount of a compound of claim 1 also disclosed, in the Venugapalan et al article.

No description of compound 15's Akt inhibitory activity is provided in the Venugapalan et al article, but a compound's pharmacological effects cannot be divorced from the compound itself. Since the compound 15 (which is embraced by instant claim 1) was administered to a mammal, inhibition of Akt is inherent because Akt is present in mammalian cells.

Claim Objections

In addition to the rejection set forth hereinabove, instant claims 6-8 are objected to because of a recurrent spelling error in compounds which include the fragment "benzimidazole" in the name. Most of these benzimidazole-containing compounds' names are misspelled "benzamidazole."

Also in claim 6, at page 33 of the Preliminary Amendment filed 28 July 2005, the second-to-last named compound on the page includes a spelling error in the name "Piperidin" is misspelled as "piepridin."

Additonally, at least one occurrence of a misspelling of "imidazole" is in the claim set. The fourth named compound in claim 7 misspells "imidazole" as "imadazole."

Claim 18 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 9. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The product-by-process language of instant claim 18

describes exactly the composition according to instant claim 9; the claims do not differ in scope.

Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because a non-initialed and non-dated alteration has been made to the address of co-inventor Mark E. Duggan. See 37 CFR 1.52(c).

Specification

The disclosure is objected to because of a recurrent spelling error in most of the compounds named which include the fragment "benzimidazole." In the instant specification, "benzimidazole" is misspelled as "benzamidazole."

Additonally, at least one occurrence of a misspelling of "imidazole" is in the specification. The last compound named on page 40 of the specification includes this spelling error. Appropriate correction is required.

Allowable Subject Matter

No prior art disclosing any compounds according to claims 2-8 or pharmaceutical compositions according to claims 10 and 11 was discovered in the search and examination.

Upon the filing of a proper Terminal Disclaimer over copending Application No. 10/510,068, the double patenting rejection will have been overcome, at which time claims

2-8, 10 and 11 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Cancellation of claims 12-18, 24 and 25 is recommended so as to overcome the enablement rejections and duplicate claim.

The Venugapalan et al references cited herein constitute the closes prior art with respect to compounds according to claims 2-8.

Also of interest, is US 7,034,026 (Barnett et al), which discloses 2,3-diphenylquinoxaline Akt inhibitors similar to those according to the present invention, except that the compounds disclosed therein lack the "Q"-variable-containing moiety.

Conclusion

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Monday to Friday from 5:45am to 2:15pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Zachary C. Tucker
Primary Examiner
Art Unit 1624